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Genotoxic effects of metabolic derivatives of the new drug phosphabenzide

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Abstract

Genotoxic action of four possible metabolites of the new tranquilizer phosphabenzide (acetylphosphabenzide, diphenylphosphinylacetic acid, phosphabenzide hydrazone with pyruvic acid, bis-1,2-(diphenylphosphinylacetyl)hydrazine) has been studied. These metabolites belong to slightly toxic phosphororganic compounds. The Ames Salmonella/microsomes tests performed on strains TA100 and TA98 showed that of these compounds only acetylphosphabenzide possessed mutagenic action. Metabolic activation of liver microsomes decreased the mutagenic effect. The mechanism of action of acetylphosphabenzide is likely to involve the formation of acetylhydrazine, capable of producing active electrophiles attacking DNA.